

#29/12

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Galdes et al.

Serial No: 09/435,733

Filed: November 8, 1999

For: Methods and Compositions for
Treating or Preventing Peripheral
Neuropathies

Attorney Docket No. CIBT-P02-052

Art Unit: 1646

Examiner: M. Brannock

Commissioner of Patents
Washington, D.C. 20231

Declaration Under 35 U.S.C. §1.132 of Karen Allendoerfer

Sir:

I, Karen Allendoerfer of Massachusetts, hereby declare as follows:

1. I am an employee of Curis Inc., the assignee of record.
2. Experiments were performed in collaboration with me, the results of which are depicted in Exhibits A-C, which demonstrate the role of hedgehog signaling in diabetic neuropathy and the effects of treating adult, diabetic rats with *sonic hedgehog*. We note that in these experiments, diabetes was induced in adult male rats with an intraperitoneal injection of streptozotocin (STZ), and rats were treated with a modified form of human Sonic hedgehog in which the N-terminal cysteine was replaced by two isoleucine residues (II-Shh). Exhibit A shows in situ hybridization analysis which indicates that *desert hedgehog* is expressed in adult peripheral nerves, and this expression is severely reduced in the nerves of diabetic rats. Exhibits B and C show that administration of *sonic hedgehog* improves both sensory nerve conduction velocity (SNCV) and motor nerve conduction velocity (MNCV) in diabetic rats. In Exhibit B, filled squares represent vehicle treated control animals, open squares represent Shh treated control animals, filled circles represent vehicle treated diabetic animals, and open circles represent diabetic animals treated with 1.0 mg/kg Shh.
3. The above experiments were performed in accord with the teachings of the abovementioned patent application.
4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these

statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Karen L. Allendoerfer
Karen Allendoerfer

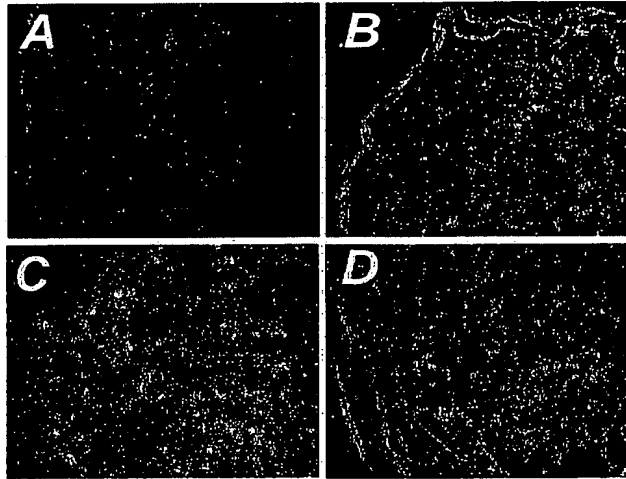
Dated: 12 November 2002



Diabetic

dhh

β-actin



Non-Diabetic

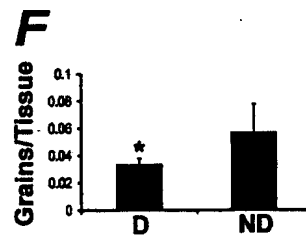


Exhibit A

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Fig. 3

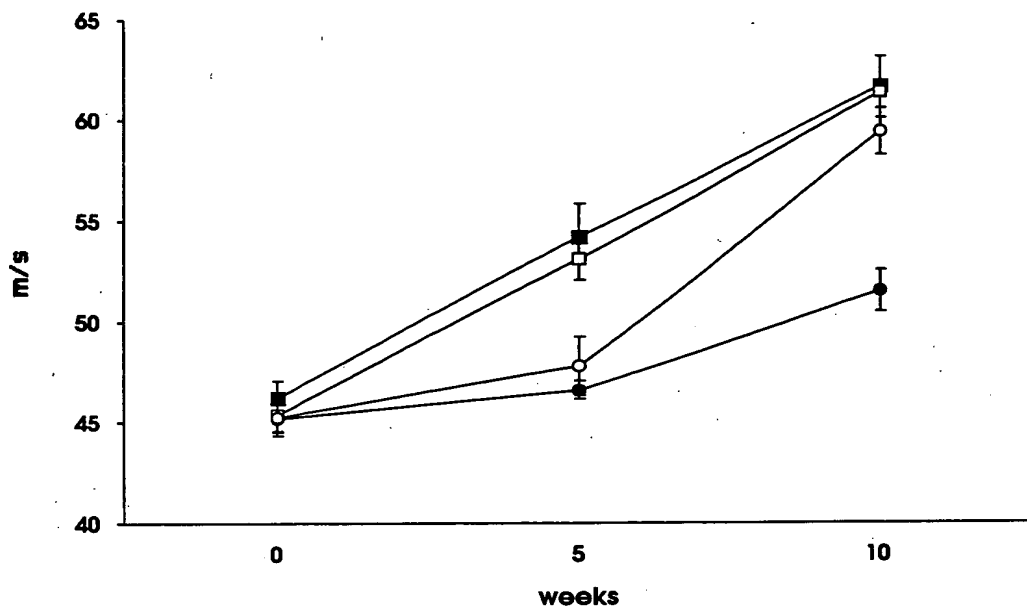
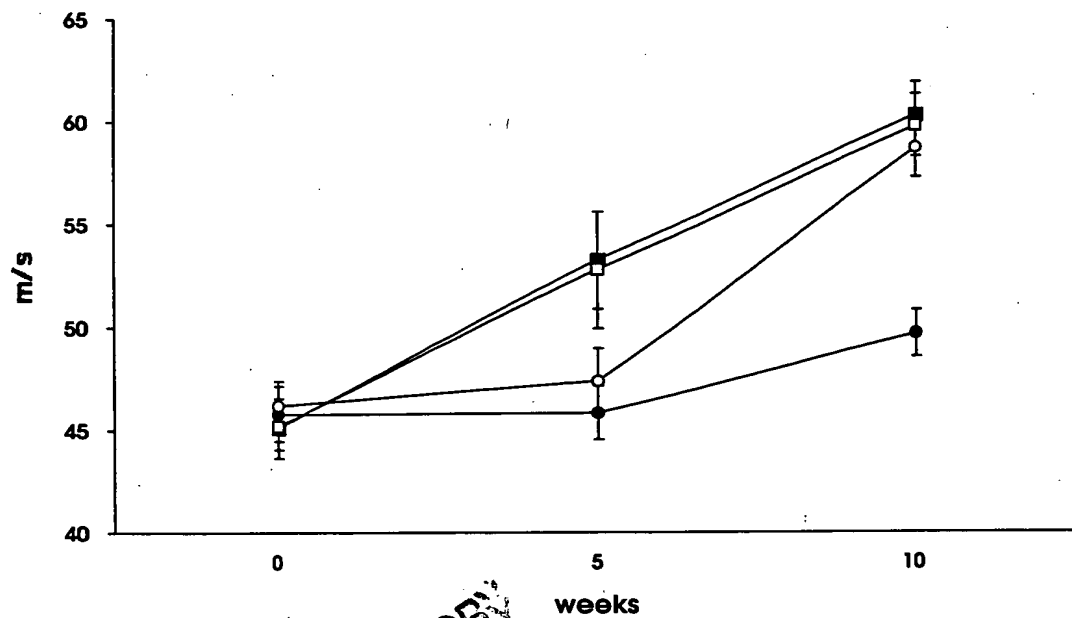


Fig. 4



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Exhibit C

		MNCV (m/sec)	SNCV (m/sec)
control + vehicle		60.4 +/- 2.4	58.7 +/- 3.7
diabetic + vehicle		44.6 +/- 3.9	42.1 +/- 3.5
diabetic + Shh (0.3 mg/kg)		54.9 +/- 8.6	55.1 +/- 4.2
diabetic + Shh (3.0 mg/kg)		62.3 +/- 6.7	61.5 +/- 4.4

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